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# FURTHER STUDIES OF DAPHNIPHYLLINE

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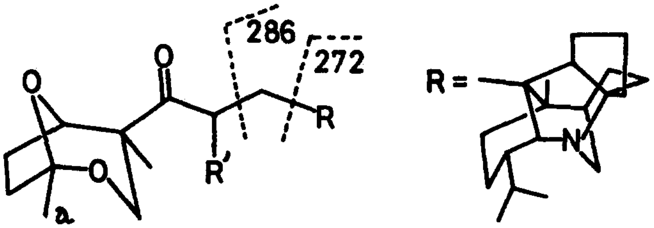
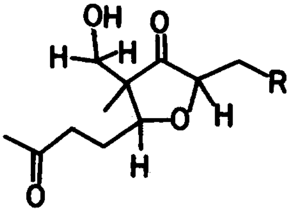
In the previous paper (1, 2), we reported the structure of daphniphylline (Ia). During our studies of the transformation of daphniphylline into the other minor alkaloids, which were isolated from the same plant, we found some interesting reactions. When treated with 6N-hydrochloric acid at 80°C for 45 min (3), daphniphylline as well as desacetyl-daphniphylline (Ib) was converted into white solid, desacetyl-isodaphniphylline (m/e 485 ($M^+$), 455 ($M^+$- 30), 286 and 272 (a pair of characteristic peaks, as shown in I); $\nu_{max}^{KBr}$ 3400 (OH), 1753 (five-membered ring ketone) and 1714 $cm^{-1}$; no acetoxyl group) in quantitative yield. In the NMR spectrum of desacetyl-isodaphniphylline, in addition to four methyl signals in the 0.90 - 1.15 ppm region, a sharp singlet (acetyl group) at 2.14 ppm was observed instead of a methyl singlet (a) at 1.41 ppm of Ia. Furthermore, there are an AB quartet (2H, J = 11 cps) centered at 3.49 ppm and multiplets (2H) at the 4.00 - 4.30 ppm region. On the basis of the above spectral data (IR, NMR and mass spectra), desacetyl-isodaphniphylline should have the structure II or III, which was formed through an intermediate IV. Desacetyl-isodaphniphylline hydrochloride was acetylated with acetic anhydride and pyridine to give an isodaphniphylline hydrochloride, m.p. 197 - 198.5°C ($C_{32}H_{49}O_5N\cdot HCl$

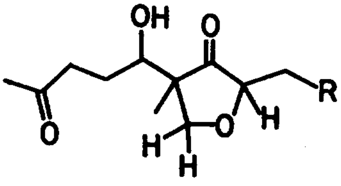


(Ia, R' OAc); (Ib, R' OH); (Ic, R' H)

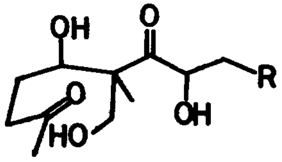
requires: C, 68.12; H, 8.93; N, 2.48. Found: C, 68.36; H, 8.88 and N, 2.59%; m/e 527 ($M^+$), 286 and 272 (a pair of characteristic peaks in I); $\nu_{max}^{KBr}$ 2600 br., 1756, 1744, 1709 and 1231 $cm^{-1}$; no hydroxyl band) in 73% yield (4). Isodaphniphylline hydrochloride was also obtained by treatment of desacetyl-isodaphniphylline hydrochloride with only acetic acid at 95°C for 21 hrs in 66% yield. The NMR spectrum of isodaphniphylline is shown in Fig. 1. In the NMR spectrum of isodaphniphylline, in addition to the presence of an acetoxyl signal at 2.00 ppm, an AB quartet at 3.49 ppm in desacetyl-isodaphniphylline was shifted to an AB quartet centered at 3.99 ppm (2H, J = 11 cps). From the above result, isodaphniphylline should have the structure V.



(II)



(III)



(IV)

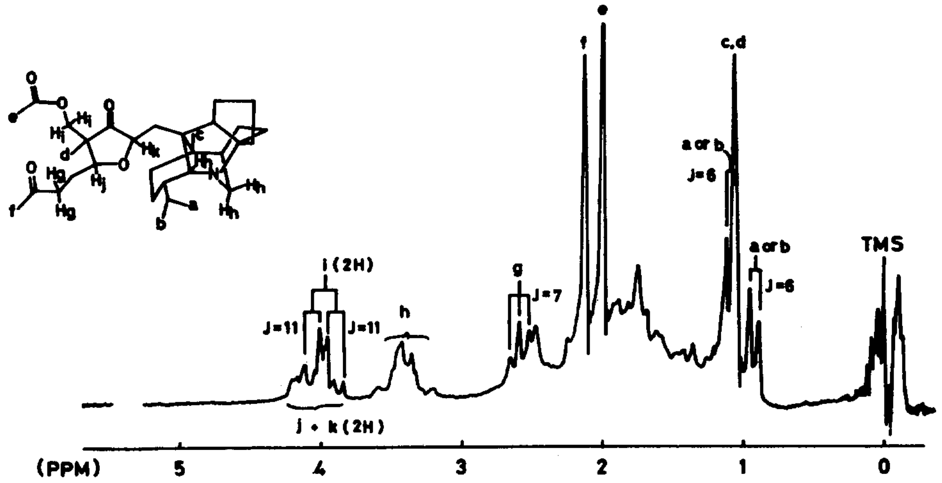
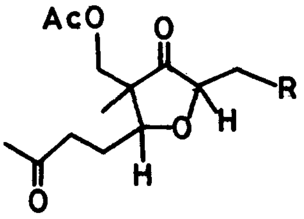
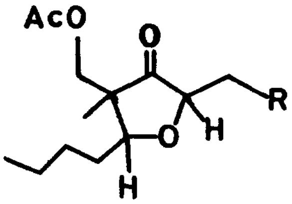


Fig. 1. The NMR spectrum of isodaphniphylline.

When isodaphniphylline was stirred with active zinc powder in acetic anhydride saturated with dry hydrogen chloride gas at room temp. overnight, an $\alpha$-ether oxygen-carbon bond was not cleaved, but the methyl ketone was reduced to form an unexpected desoxy-isodaphniphylline hydrochloride (VI) (m.p. 212 - 214°C (in a sealed tube); m/e 513 ($M^+$), 286 and 272 (a pair of characteristic peaks in I); $\nu_{max}^{KBr}$ 2600 br., 1755 br. and 1230 cm$^{-1}$; no hydroxyl band) in 46% yield. The NMR spectrum of VI is shown in Fig. 2. In the comparison of the NMR spectra of isodaphniphylline and desoxy-isodaphniphylline, the latter has five methyl signals in the 0.90 - 1.15 ppm region and only one acetoxyl signal at 1.99 ppm. On the other hand, the former has four methyl signals in the 0.90 - 1.15 ppm region, an acetoxyl signal at 2.00 ppm and an acetyl signal at 2.13 ppm. The above spectral data supported structure VI for the reduction product, in which the sterically hindered five membered ring ketone was remained. Under the same conditions



(V)



(VI)

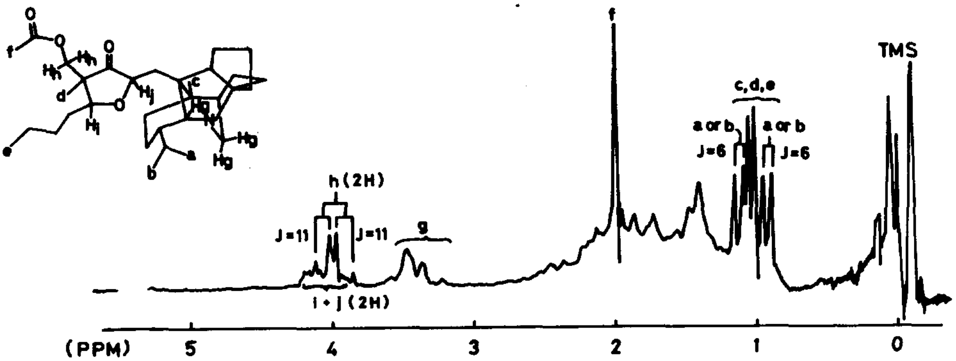


Fig. 2. The NMR spectrum of desoxy-isodaphniphylline

described above, cholestan-3-one was also reduced with active zinc powder in acetic anhydride saturated with dry hydrogen chloride gas to cholestane, in a Clemmensen-type reduction. This reduction system seems to be pretty convenient for the conversion of ketones to methylene groups. Studies are now in progress to find the optimum conditions for the conversion of ketones to methylene groups with the same reduction system.

Chemical shifts of all NMR spectra are given in ppm from an internal TMS standard using $CDCl_3$ as a solvent unless otherwise stated.

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## REFERENCES

1. N. Sakabe, H. Irikawa, H. Sakurai and Y. Hirata, Tetrahedron Letters **9**, 963 (1966).
2. N. Sakabe and Y. Hirata, Tetrahedron Letters **9**, 965 (1966).
3. Codaphniphylline (Ic, R = H) was recovered under the same reaction condition as that of daphniphylline (Ia, R = OAc).
4. Desacetyl-isodaphniphylline was obtained quantitatively from isodaphniphylline by treatment of the latter with 6N-hydrochloric acid at 80°C for 45 min.